SUPPLEMENTAL ACTION

This action corrects the errors in the Office Action mailed 18 July 2008. A notice of references cited (Form 892) and the copies of the cited references are not included herewith as they were previously mailed with the office action of 18 July 2008. The mailing of this Office action resets the shortened statutory time period for reply to 3 months from the mailing date of this Supplemental Office Action. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 March 2008 has been entered.

Claim Status

Claims 32-52 are pending.

Claims 1-31 are cancelled.

Claims 32-52 have been examined.

Claims 32-52 are rejected.

Priority

Applicants' amendment to the specification to claim benefit to Application No. 09/981, 248 is acknowledged.

Information Disclosure Statement

The information disclosure statements (IDSs) submitted on 11 April 2008 comply with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 49-52 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 49-52 are drawn to a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998) below, the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result:

> The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to -- process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Section 101 specifies that statutory subject matter must also satisfy the other "conditions and requirements" of Title 35, including novelty, nonobviousness, and adequacy of disclosure and notice. See *In re Warmerdam*, 33 F.3d 1354, 1359, 31 USPQ2d 1754, 1757-58 (Fed. Cir. 1994). For purpose of our analysis, as noted above, claim 1 is directed to a machine programmed with the Hub and Spoke software and admittedly produces a "useful, concrete, and tangible result." *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557. This renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be “useful,” the claim must produce a result that is specific, and substantial. For a claim to be “concrete,” the process must have a result that is reproducible. For a claim to be “tangible,” the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

Claims 49-52 do not require production of a tangible result in a form that is useful to the user of the process or apparatus. The claims are directed to a method of determining a presenting a likelihood that a person has a mutated form of a gene that results in presenting an inferred finding. The claims as a whole comprise computational steps and are thus drawn to a judicial exception, i.e. an abstract idea. The claim produces a result that is a presentation of an inferred finding. However, giving the claims the broadest interpretation reasonable, the presentation is not a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to

recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-45 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42-45 and 48 recite the limitation "The method" in line 1. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

Response to Arguments

Applicant's arguments, see Remarks p. 8-13, filed March 2008, with respect to the rejection of claims 32-52 as anticipated by Kobrinskii et al. as evidenced by Steadman's medical dictionary under 35USC 102(b) have been fully considered. The rejection of claims 32-52 has been withdrawn in view of amendments to the claims.

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, see Remarks p. 13-17, filed 10 Mach 2008, with respect to the rejection of claims 32-52 as unpatentable over Pathak et al. under 35 USC 103(a)

have been fully considered. The rejection of 32-52 has been withdrawn in view of the amendments made to the claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 32-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pathak et al., in view Yan et al. (Drug Information Journal, Vol. 34, pp. 1247-1260, 2000), Roses (Nature, Vol. 405, p. 857-865, 15 June 2000), and Wolf et al. (British Medical Bulletin, Vol. 55, No. 2, p. 366-386, 1999) and in view of Kobrinskii et al.

The claims are directed to a method (claims 32-40 and 49-52) and system (claims 41-48) of determining the probability that the a person has a gene mutation by receiving a prescription for a patient from a clinician; determining if the prescribed agent or event is correlated with a gene; querying a database to determine if the patient has genetic results consistent with the correlated gene; if the genetic test results do not exist, obtain the route of inheritance for the gene; query a database to identify any family members with genetic test results with the route of inheritance; use the genetic results of the identified family members to calculate the probability that the patient has a gene mutation; report the probability that the patient has a gene mutation.

Pathak et al. teach a computerized method and system for automatically reporting genetic risk, i.e. the probability of a gene mutation. The method of Pathak et al. relies on case data for a patient. The system analyzes the data and produces a probability of the presence of a mutation. The input of case data as depicted in fig. 1 conceptually demonstrates data that is stored and utilized by the system, thereby reading on the limitation of a database. Consistent with the limitation of a database is the blackboard (p.165, col. 2, para. 1), a global data structure. Pathak et al. teach the input as a set of objects each having the attributes name, sex, parents, siblings, spouse, children, loci (p.165, col. 2, para. 1). The attribute *loci*, as Pathak et al. teach, is a set of

alleles in the genome reading on the limitation of genetic test results (p.165, col. 2, para. 1). Pathak et al. teach the use of rule sets to define queries of the case data to identify the route of inheritance based on familial relationships as well as to utilize the loci information to calculate a probability of an allele's presence (p.165, col. 2, para. 2 and p. 166, col. 2, #8). Pathak et al. shows genetic risks influence medical decisions (p. 169, col. 2). Regarding claims 34 and 43, Pathak et al. teach knowledge source 2 concerned with allele inheritance relations with in the pedigree (p. 165, col. 2, "allele flow"). Regarding claims 35 and 44, Pathak et al. teach calculating the likelihood the individual has a mutated form of the gene using the genetic markers (alleles) of at least one family member (p. 166, col. 2, "possible–explanations" and "Bayesian-analysis"). Regarding claim 36, Pathak et al. teach a computer readable media comprising the instructions for the method (p. 169, col. 2, para 2, "software"). Regarding claim 39 and 48, Pathak et al. teach the example of x-linked mode of inheritance (p. 167, col. 1, "X-linked"). Regarding claims 33, 40, 42 and 45, Pathak et al. teach that all a user must do is provide the system with the relevant data (p. 169, col. 1, last three lines). It is common for an individual's medical information to exist in electronic form and comprise medical data of related family members. Therefore, the teaching of providing the system with the relevant data is viewed to read on the limitations of electronic records from a comprehensive healthcare database.

Pathak et al. does not teach electronic prescription ordering where that which is prescribed is determined to be correlated with a gene or risk of atypical events. Pathak et al. doe not explicitly show a patient database and a family member database.

Yan et al. discusses the importance of electronic prescription ordering with in the context of integrated healthcare systems. Yan et al. shows that the benefit of electronic ordering systems is that the automated surveillance increases the awareness of adverse or atypical drug events (ADEs) by the clinicians and other healthcare professionals (p. 1258, col. 2). Yan shows that the nationwide cost due to ADEs is $76.6 billion annually (p. 1247, col. 2). Yan et al. shows ADEs can be divided into two classes, type A and type B (p. 1258, col. 1). Type A reactions are those reactions caused by known drug toxicities. Type B reactions are those reactions caused by allergic and other idiosyncratic reactions. Yan et al. suggests that type B reaction can be prevented using pharmacogenomics/pharmacogenetics (p. 1258, col. 2). Yan et al. shows the importance a computerized order entry system, one that provides the necessary interactive information about drugs, patients, laboratory data, drug-drug interactions, and drug-patient interactions, combined with prescribing guidelines (p. 1253, col. 2). Yan et al. shows in table 4a that elements of computer systems that prevent ADEs at the prescription stage of drug ordering do so by providing decision-support systems, patient-specific (demographic, drug allergies, radiology orders, and laboratory test results) and disease-specific information, a reduction in errors by facilitating access to information, and monitoring of laboratory results. Yan et al. shows a patient database (p. 1256, col. 1) Yan et al. continues to show that the database is used to determine the likelihood of a treatment leading to an ADE (p. 1256, col. 1). Regarding claims 38 and 47, presenting an alert to a user, if the gene variant is indicative of an atypical event, Yan et al. shows an electronic prescribing system that

includes information on known drug allergies and provides alerts to clinicians (p. 1257, col. 2). Yan et al. shows ADEs can be divided into two classes, type A and type B (p. 1258, col. 1). Type A reactions are those reactions caused by known drug toxicities. Type B reactions are those reactions caused by allergic and other idiosyncratic reactions. Yan et al. suggests that type B reaction can be prevented using pharmacogenomics/pharmacogenetics (p. 1258, col. 2). Yan et al. further suggests alerting the user/clinician of ADEs based on gene variant detection (p. 1259, col. 1).

Roses shows the application of pharmacogenetics research to clinical practice, physicians will be able to use information from patients' DNA to determine how patients are likely to a particular medicine (p. 860, col. 1). Roses suggests that metabolic screens of genetic variants will be standardized so that automated readouts of each persons predicted response to each medicine could be generated and will be useful to aid in individual dosing and avoidance of side effects (p. 860, col. 1). Roses suggests that using pharmacogenetics, medicines would be prescribed to only those patients where a high probability (likelihood) of efficacy without significant adverse or atypical events is expected (p. 863, col. 1). Roses shows the benefit of the application of pharmacogenetics to the delivery of medicines will maximize the value of each medicine (p. 863, col. 1). Roses shows that pharmacogenetics will beneficially effect the economy of predictable efficacy, limited adverse events, lower complications owing to targeted delivery, and increased cost-effectiveness of medicines to improve health-care delivery and eliminate the need for rationing (p. 863, col. 2). Roses shows that pharmacogenetic profiles predict if an individual patient is likely to benefit from a

medicine and be free of serious side effects (p. 864, figure 5 legend). Regarding claims 37 and 46, the determination of gene variant that is indicative of atypical event, Roses suggests that by using pharmacogenetics, medicines would be prescribed to only those patients where a high probability (likelihood) of efficacy without significant adverse or atypical events is expected (p. 863, col. 1).

Wolf et al. shows that genetic variation results in an observed variability in drug response related to absorption disposition metabolism and excretion. Wolf et al. shows the identification of the molecular basis of pharmacogenetic polymorphisms and the ability of screen individuals for the presence of specific alleles opens up the possibility of screening patients to predict drug out come and allow individualized drug treatment based on genetic constitution. Wolf et al. shows that certain drugs are metabolized by one or more polymorphic p450 (table 1). Wolf et al. show by way of example that a polymorphism at the CYP2D6 gene locus was identified from the observation that certain individuals are 'ultra-rapid' metabolizers that do not respond to therapy with drugs which were CYP2D6 substrates. Wolf et al. shows the non-responder effect is due to an inherited amplification of the CYP2D6 gene that is overcome by significantly elevated doses of CYP2D6 drugs (p. 376-377).

Kobrinskii et al. shows the computerization of medical genetic information to result in an integrated healthcare information system having a client-server architecture. Kobrinskii et al. shows the system has patient database in the in form of patient medical cards (p. 172). Kobrinskii et al. shows that the system also has a family member data base in which genetic information for family members of the patient is stored and

queried automatically to generate a likelihood the patient has a mutation (p. 172). Kobrinskii et al. shows the system has the advantage of improving medical documentation and providing high quality medical help to families with inherited diseases (p. 173).

Regarding claims 49-52, the limitations are taught in part as above.

It would have been obvious to apply the method/system for genetic risk assessment of Pathak et al. with the electronic prescribing systems of Yan et al. to practice the instant invention because Yan et al. shows that the benefit of electronic ordering systems is that it increases the awareness of adverse or atypical drug events (ADEs) by the clinicians and other healthcare professionals and suggests that type B adverse reactions can be prevented using pharmacogenomics/pharmacogenetics. It would have been further obvious to modify the method/system for genetic risk assessment of Pathak with the pharmacogenetic/pharmacogenomic information of Roses because Roses suggests that using pharmacogenetics, medicines would be prescribed to only those patients where a high probability (likelihood) of efficacy without significant adverse or atypical events is expected. It would have been further obvious to modify the method/system for genetic risk assessment of Pathak with the pharmacogenetic/pharmacogenomic information of Wolf et al. because Wolf et al. shows the identification of the molecular basis of pharmacogenetic polymorphisms and the ability of screen individuals for the presence of specific alleles opens up the possibility of screening patients to predict drug out come and allow individualized drug treatment based on genetic constitution. It would have been further obvious to modify

the method/system for genetic risk assessment of Pathak with the computerization of medical genetic information to result in an integrated healthcare information system having a client-server architecture of Kobrinskii et al. because Kobrinskii et al. shows the system has the advantage of improving medical documentation and providing high quality medical help to families with inherited diseases. One would have been motivated to do so because Pathak et al. teach the method/system allows the study of any given case with any number of observations and assumptions, the system streamlines the computation of risk which are used to make critical medical decisions and method/system automates error-prone, complex, tedious process to be a valuable aid to clinicians.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32-39, 41-47, and 49-52 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 10/826563. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application is directed to a method and system for determining the likelihood a person has a mutation or genetic variant of a gene that is associated with a treatment. In some embodiments, the instant application also determines the risk associated with the patient to suffer an atypical event. Similarly, Application No. 10/826,563 is directed to a system and method for the determination of the likelihood that a person has a mutation or genetic variant that is indicative of a risk of an atypical event.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

A shortened statutory period for reply to this action is set to expire THREE MONTHS from the mailing date of this action. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571) 272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

19 October 2008

/K. R. S./
Examiner, Art Unit 1631

/Marjorie Moran/
Supervisory Patent Examiner, Art Unit 1631